KH_2PO_4 than in H_2O was reported by Tonya M. Herne and Michael J. Tarlov (Herne TM and Tarlov MJ, Characterization of DAN Probes Immobilized on Gold Surfaces. J. Am. Chem. Soc. 1997, 119, 8916-8920). For coating the sensor surface with the capture oligonucleotide sequence, 100 µl of 2 µM capture oligonucleotide were added to each sensor and incubated at room temperature for 2 hours, followed by wash with phosphate buffered saline (PBS). After wash, the sensor surface was blocked with 0.3% BSA for 30 min followed by wash with PBS. For DNA hybridization, 100 µl of either 1 nM wildtype or 1 nM mutant oligonucleotide sequences in hybridization buffer (1.0 M NaCl with 10 mM Tris buffer, pH 7.4 and 1 mM EDTA) were added to the capture oligonucleotide-coated sensors. For negative control, no DNA target was added. Hybridization was carried out at 42°C for 30 min followed by wash with phosphate buffer with 50 mM NaCl. For detection of DNA hybridization and discrimation of single nucleotide substitution, 100 µl of streptavidin labeled alkaline phosphotase (1:2000 dilution in Tris buffer) was added to each senor and incubated for 30 min at room temperature followed by wash with Tris buffer. After wash, 100 µl of an alkaline phosphotase substrate mix, BCIP/BNT was added and the reaction was monitored on the impedance analyzer in real time. As shown in the figure, the specific hybridization between the capture sequence and the wildtype target sequence can be steady detected on the electronic device, the signal for which is 92.6 fold higher than the signal generated from the negative control sensor at 60 min. Here the signal is the resistance measured 5 kHz between electrode structures in each well. Notably, the mutant sequence with single nucleotide substitution generated very weak signal compared to its wildtype sequence. The signal difference at 60 min between the wildtype sequence and the mutant sequence is 30 fold.

REMARKS

The amendment to the specification amends paragraph **[0075]** on pages 21-22, by removing the two nucleotide sequences of the paragraph and replacing them with a description of the sequences by referring to the Genbank sequence they are derived from. This amendment adds no new matter.

Paragraph **[0075]** is part of the 'BRIEF DESCRIPTION OF THE DRAWINGS' section of the application. The amended paragraph refers to Figure 21. Figure 21 presents in the form of a graph data showing that a device of the present invention can be used for nucleic acid detection using hybridization in which a capture oligonucleotide is bound to the sensor surface of the device, and hybridization is performed with a wildtype and a mutant oligonucleotide. The capture nucleotide, listed in the paragraph as (1), is now described in terms of its residue numbers in the Genbank sequence, rather than listing the sequence itself. The wildtype probe (2) is also now referred to in terms of its complementarity to a sequence of residues in the Genbank sequence, rather than listing the sequence itself. The mutant oligonucleotide probe (3) is now referred to in terms of the single nucleotide change it has with respect to (2), as it was before, and additionally refers to the residue number of the Genbank sequence for the mutated nucleotide.

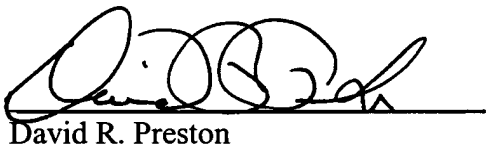
The disclosed sequences are provided in an example of use of a device of the invention and are not claimed. This amendment obviates the need to provide Sequence Listings for oligonucleotides (1) and (2).

CONCLUSION

Applicants respectfully submit that the specification and claims are ready for examination and in condition for allowance.

Respectfully submitted,

Date: Jan 27, 2005



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